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Published

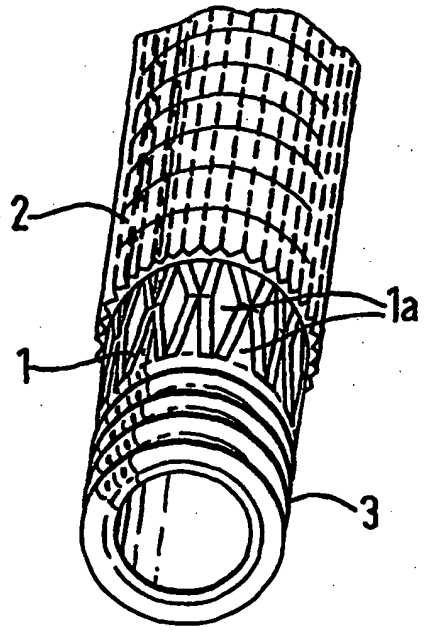
With international search report.

Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: ENDOLUMINAL STENT

(57) Abstract

An endoluminal stent has a core (1) of stainless steel which has an expandable capability through the provision of slits which form interstices (1a) after assisted or self-expansion following which the core is sufficiently rigid to support the vessel into which it is inserted. The core (1) is shown here in a partially expanded state. The core (1) has an outer covering (2) of a material such as Dacron or PTFE which is coated on surface with an agent or agents such as collagen or gelatin, in order to decrease the material porosity and enhance incorporation into surrounding tissues. This coating in itself may be bonded with or incorporate a therapeutic agent or agents such as Heparin or an antibiotic. Internally the core (1) includes a lining (3) of a material similar to the outer covering layer and this may also be coated with an agent or agents such as collagen or gelatin, in order to decrease the material porosity and enhance incorporation into surrounding tissues. The outer covering and the lining are joined around the ends of the core. The stent thus provides smoothed blood flow as well as reducing restenosis due to muscle cell growth as well as offering a means for long term delivery of a therapeutic agent.



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TITLE

Endoluminal Stent

This invention relates to an improved construction of an endoluminal stent, such devices being used for example, to hold open blood vessels dilated by angioplasty, particularly blood vessels having a higher flow, such as the iliac arteries. However, endoluminal stent devices may be deployed elsewhere in the mammalian body (usually human) for example, along the length of the gut, the bile duct, the pancreatic duct or the urethra. Such devices usually comprise a tubular cage structure which is inserted collapsed into a blood vessel, or other tubular structure, and thereafter expanded using a balloon catheter or using the self-expanding properties of the alloy from which it is constructed, for example. Stent devices having an open lattice structure are used normally with the lattices providing for expansion of the stent after insertion. A disadvantage of such constructions, however, is that the interstices allow for smooth muscle cell growth to invade through the stent, thus once again blocking the lumen.

To help counter this effect, it has been proposed previously to provide a form of covering over the stent in order to "close-off" the interstices.

Thus, it has been proposed for example, to provide a stent device which is embedded completely within a PTFE covering and whereby the covering yields and expands with the stent itself when deployed.

One of the objects of this invention is to provide an endoluminal stent giving an improved blood flow and longer *in situ* therapeutic life.

A further and preferred object of this invention is to provide a stent which is

capable of delivering a therapeutic agent or agents over a period of time. Such an agent might be directed specifically at preventing the growth of smooth muscle cells locally.

In a preferred embodiment this invention seeks to provide an endoluminal stent giving an improved blood flow over the surface that would, in addition, prevent re-stenosis of the arterial lumen due to the growth of muscle cells through the interstices of said stent. However, growth of cells around the ends of such a stent device would still not be prevented and which, in turn, may cause a re-stenosis of the lumen.

Broadly, and in accordance with a first aspect of this invention, there is provided an endoluminal stent having a rigid or semi-rigid, preferably metallic, self-supporting tubular core which may be expanded outwardly and including an outer expandable, preferably a porous or semi-porous, absorbent or fabric covering and an inner expandable, preferably a porous, absorbent or fabric lining, the covering and the lining being joined or continuous around the ends of the tubular core.

In a modification, and also according to this invention, there is provided a stent with open interstices, that is without the coverings, which interstices are filled with a bio-polymer carrier substance

The linings, within and without, may or may not in themselves be covered with a bio-polymer carrier medium for example, collagen or gelatin and may be a fabric material either of a woven or non-woven kind, such as Dacron (a Trade Mark), or an expandable material such as PTFE. Other materials may be used such as polyurethanes.

Broadly, and in accordance with a second aspect of this invention, there is provided an endoluminal stent comprising a preferably metallic self-supporting core with a plurality of regularly or irregularly extending slits or cuts running longitudinally along the core whereby the core may be expanded such that the slits open up to define the interstices with preferably an outer covering of an expandable material provided over the core and an internal expandable lining within the core, one or other or both of said coverings or linings being capable of both part-retaining and permitting diffusion of a therapeutic agent or agents held therein retained in the slits or interstices of the core, preferably incorporated or held within a biologically inert, biodegradable bio-polymer. Said bio-polymer, or similar, holding or incorporating a therapeutic agent or agents in both the metallic framework of the stent device core in addition to being located within the now expanded interstices of the device.

The construction according to a first aspect of this invention thus provides for a covering and lining of a fabric material to be provided preferably on both external and internal surfaces of the stent, thus preventing external intrusion through the interstices of the rigid core as well as improving blood flow through the internal passage formed by the core.

In the second aspect of this invention, provision is made for incorporating a therapeutic agent or agents, with or without a bio-polymer carrier medium, in or between the two coverings such that the agent or agents may be retained in the slits or interstices of the core to be diffused over a period of time following insertion of the stent into a blood vessel or other tubular structure.

The therapeutic agent or agents may be carried, for example, by means of

an impregnated collagen sponge or gel film or the like which may form an additional layer preferably enclosed on both sides by the coverings or linings. Other carriers may be used to hold the therapeutic agent or agents.

Further and preferred features of this invention together with one practical construction will now be described in the following and by reference to the accompanying drawings, wherein:

Figure 1 shows in side elevation a stent with a part of the core and the outer covering removed for clarity, and

Figure 2 shows an end elevation of the stent shown in Figure 1.

Referring to the drawings, the endoluminal stent of this invention includes a core 1 of stainless steel or an alloy such as nitinol which has an expandable capability. The construction is such that after assisted or self-expansion, the core is sufficiently rigid to support the vessel into which it is inserted. The core 1 is shown here in a partially expanded state. Interstices or the spaces between the metal parts are here referenced 1a.

According to this invention the core 1 has an outer covering 2 of a material such as Dacron or PTFE. Where Dacron material is used, this may be coated on a single surface or both surfaces with an agent or agents such as collagen or gelatin, in order to decrease the material porosity and enhance incorporation into surrounding tissues. This coating in itself may in turn be bonded with or incorporate a therapeutic agent or agents such as Heparin or an antibiotic.

Internally, the core 1 includes a lining 3 of a similar or other material to the outer covering layer. Where Dacron material is used, this may be coated on a single surface or both surfaces with an agent or agents such as collagen or

gelatin, in order to decrease the material porosity and enhance incorporation into surrounding tissues.. This coating in itself may in turn be bonded with or incorporate a therapeutic agent or agents such as Heparin or an antibiotic.

The outer covering layer may be connected with the inner lining layer at spaced locations by means of suitable glueing, suturing or welding or contact by any other means. At the ends of the stent the covering and lining may also be joined over and around the end of the core by using such means or by using stitching thereby sealing in the metallic core completely. This will provide potential space for retention of an appropriate therapeutic agent or agents which may be carried between the interstices of the core 1 and passed through either the outer covering and/or the lining. With such an arrangement a therapeutic agent or agents may be diffused over a period of time into the surrounding arterial wall or if appropriate, into the bloodstream or into the wall of another tubular structure.

It is thus a particular feature of this invention to provide a stent device incorporating a therapeutic agent or agents which is retained within the stent structure, that is within the interstices and/or over the metallic parts, to be diffused into the surrounding arterial wall (or bloodstream if appropriate) during the useful life of the device or part thereof.

The material used to cover the metallic stent core should have certain expansible properties.

In a further embodiment the outer covering 2 and lining 3 may be bonded by means of any substance which holds the coverings together through the interstices in the core 1. In this construction the bonding agent or agents itself

may incorporate a required therapeutic agents.

This invention also contemplates a method of treatment of the body and particularly any blood vessel or other tubular or elongate structure, for example a urethra or bile duct or other part of the gastro-intestine tract or uro-genital tract, which comprises the insertion of an endoluminal stent substantially as hereinbefore disclosed with the stent device incorporating means for retention of a therapeutic agent or agents, the agent or agents being effective on an ongoing basis following insertion of the stent.

According to another aspect of this invention there is provided the use of an endoluminal stent substantially as described and disclosed herein for the purpose of administering a therapeutic agent or agents to the flow of blood through a vessel in a mammalian body or other tubular or elongate structure, for example a urethra or bile duct or other part of the gastro-intestine tract or uro-genital tract.

CLAIMS:

1. An endoluminal stent having a rigid or semi-rigid self-supporting tubular core which may be expanded outwardly and including an outer expandable, absorbent or fabric covering and an inner expandable absorbent or fabric lining, the covering and the lining being joined or continuous around the ends of the tubular core.

2. An endoluminal stent according to claim 1, wherein the core is metallic and/or the outer covering is porous or semi-porous and/or the inner lining is porous.

3. An endoluminal stent according to claim 1 or 2, wherein the covering and the lining are covered with a bio-polymer carrier medium, preferably collagen or gelatin, the covering and the lining being a fabric material either of a woven or non-woven kind or an expandable material such as PTFE or a polyurethane.

4. An endoluminal stent according to any preceding claim, wherein the covering and/or the lining incorporate a therapeutic agent or agents.

5. An endoluminal stent according to and preceding claim, wherein the core includes interstices facilitating expansion, said interstices holding a therapeutic agent.

6. An endoluminal stent comprising a metallic self-supporting core with a plurality of regularly or irregularly extending slits or cuts running longitudinally along the core whereby the core may be expanded such that the slits open up to define interstices, the core supporting preferably an outer covering of an expandable material provided over the core and an internal expandable lining within the core, one or other or both of said coverings or linings being capable of both part-retaining and permitting diffusion of a therapeutic agent or agents held therein and/or retained in the slits or interstices of the core.

7. An endoluminal stent according to claim 6, wherein the therapeutic agent is incorporated or held within a biologically inert, biodegradable bio-polymer, the said bio-polymer, or similar, holding or incorporating a therapeutic agent or agents in both the metallic framework of the stent device core in addition to being located within the expanded interstices of the device.

8. An endoluminal stent according to claim 6 or 7, wherein the therapeutic agent or agents, with or without a bio-polymer carrier medium, are located in or between the two coverings such that the agent or agents are retained in the slits or interstices of the core to be diffused over a period of time following insertion of the stent into a blood vessel or other tubular structure.

9. An endoluminal stent according to any preceding claim 6 to 8, wherein the therapeutic agent or agents are carried by means of an impregnated collagen sponge or gel film or the like which may form an additional layer preferably

enclosed on both sides by the coverings or linings

10. The use of an endoluminal stent in accordance with any preceding claim or as disclosed herein for the purpose of administering a therapeutic agent or agents to the flow of blood through a vessel in a mammalian body or other tubular or elongate structure, for example a urethra or bile duct or other part of the gastro-intestine tract or uro-genital tract.

11. A method of treatment of the body and particularly any blood vessel or other tubular or elongate structure, for example a urethra or bile duct or other part of the gastro-intestine tract or uro-genital tract, which method comprises the insertion of an endoluminal stent according to any preceding claim or substantially as hereinbefore disclosed with the stent device incorporating means for retention of a therapeutic agent or agents, the agent or agents being effective on an ongoing basis following insertion of the stent.

12. An endoluminal stent substantially as herein described and as illustrated by or with reference to the drawings.

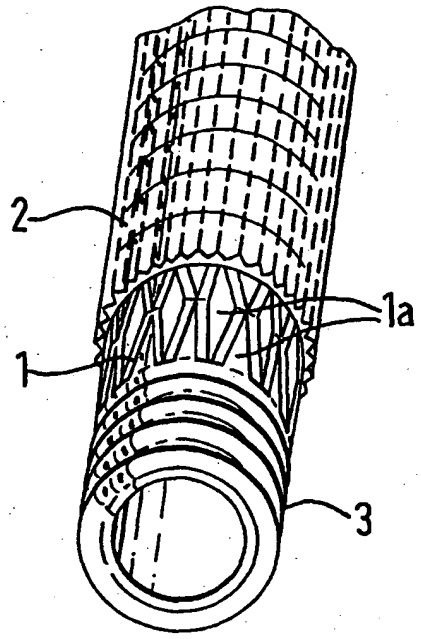

FIG. 1

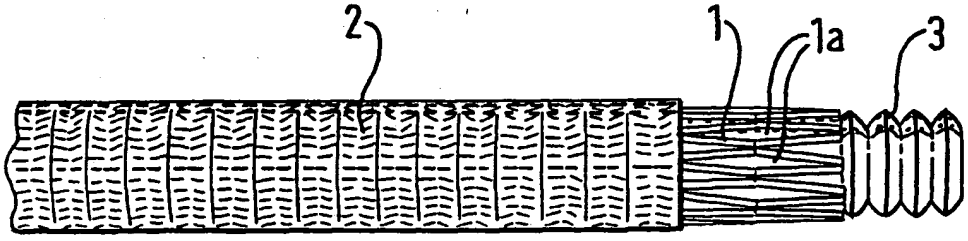

FIG. 2

INTERNATIONAL SEARCH REPORT

Int. dional Application No
PCT/GB 99/04388

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61F2/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 693 085 A (BURMEISTER PAUL H ET AL) 2 December 1997 (1997-12-02) figures 1,11-14 figures 16-20 column 3, line 31 -column 4, line 5 column 5, line 30 - line 44 column 9, line 40 - line 63 column 10, line 30 -column 11, line 12	1-4
Y	---	5,9

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
12 April 2000	28/04/2000

Name and mailing address of the ISA	Authorized officer
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Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Int ational Application No
PCT/GB 99/04388

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication.where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 23228 A (ALZA CORP) 4 June 1998 (1998-06-04) figures 1-18 page 6, line 30 -page 7, line 7 page 7, line 30 -page 8, line 11 page 8, line 25 -page 9, line 5 page 10, line 15 - line 23 page 11, line 26 -page 14, line 7 page 18, line 4 -page 20, line 24	6-8
Y	---	5,9
X	WO 97 09006 A (UNIV EMORY) 13 March 1997 (1997-03-13) page 5, line 7 - line 13 page 6, line 8 -page 10, line 23	1,2,4
A	-----	3,5,6

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 99/04388

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 10-11
because they relate to subject matter not required to be searched by this Authority, namely:
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery

2. [X] Claims Nos.: 12
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
Rule 6.2 (a) PCT

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [X] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/GB 99 04388

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-5

   An endoluminal stent having a core and an outer covering and an inner lining.

2. Claims: 6-9

   An endoluminal stent having a metallic core with a plurality of slits or cuts retaining therapeutic agents.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/GB 99 04388

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 12

Rule 6.2 (a) (PCT) : "Les revendications ne doivent pas, sauf lorsque cela est absolument nécessaire, se fonder, pour ce qui concerne les caractéristiques techniques de l'invention, sur des références à la description ou aux dessins. En particulier, elles ne doivent pas se fonder sur des références telles que "comme décrit dans la partie... de la description" ou "comme illustré dans la figure... des dessins"."

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Int .tional Application No
PCT/GB 99/04388

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5693085 A	02-12-1997	EP 0754017 A	22-01-1997
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WO 9709006 A	13-03-1997	AU 6905696 A	27-03-1997
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